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**EUROPEAN PATENT APPLICATION**

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(54) **Processes useful for nucleic acid amplification and sequencing, and for the production of nucleic acid having decreased thermodynamic stability**

(57) This invention provides novel processes for amplifying nucleic acid sequences of interest, including linear and non-linear amplification. In linear amplification, a single initial primer or nucleic acid construct is utilized to carry out the amplification process. In non-linear amplification, a first initial primer or nucleic acid construct is employed with a subsequent initial primer or nucleic acid construct. In other non-linear amplification processes provided by this invention, a first initial primer or nucleic acid construct is deployed with a second initial primer or nucleic acid construct to amplify the specific nucleic acid sequence of interest and its complement that are provided. A singular primer or a singular nucleic acid construct capable of non-linear amplifi-

cation can also be used to carry out non-linear amplification in accordance with this invention. Post-termination labeling process for nucleic acid sequencing is also disclosed in this invention that is based upon the detection of tagged molecules that are covalently bound to chemically reactive groups provided for chain terminators. A process for producing nucleic acid sequences having decreased thermodynamic stability to complementary sequences is also provided and achieved by this invention. Unique nucleic acid polymers are also disclosed and provided in addition to other novel compositions, kits and the like.

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# EUROPEAN SEARCH REPORT

Application Number  
EP 99 11 2181

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| The present search report has been drawn up for all claims  |   |  |   |
| Place of search<br>MUNICH   |   | Date of completion of the search<br>10 November 2003   | Examiner<br>Madlener, M                         |
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| Y   | US 5 270 184 A (WALKER GEORGE T ET AL) 14 December 1993 (1993-12-14)<br>* abstract *<br>* claim 1 *   | 1-32   |  |
| Y   | US 5 470 723 A (JURGENSEN STEWART R ET AL) 28 November 1995 (1995-11-28)<br>* abstract *<br>* column 3, line 49 - column 7, line 36 *<br>* figure 1 *   | 1-32   | TECHNICAL FIELDS SEARCHED (Int.Cl.6)         |
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| The present search report has been drawn up for all claims  |   |  |  |
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| The present search report has been drawn up for all claims  |  |                                  |  |                                      |
| Place of search   |  | Date of completion of the search | Examiner                                     |                                      |
| MUNICH  |  | 10 November 2003                 | Madlener, M                                  |                                      |
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| The present search report has been drawn up for all claims   |   |  |  |   |
| Place of search<br>MUNICH  |   | Date of completion of the search<br>10 November 2003 | Examiner<br>Madlener, M                      |   |
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| A   | SANGHVI Y S: "HETEROCYCLIC BASE MODIFICATIONS IN NUCLEIC ACIDS AND THEIR APPLICATIONS IN ANTISENSE OLIGONUCLEOTIDES" ANTISENSE RESEARCH AND APPLICATIONS, CRC PRESS, GB, 1993, pages 273-288, XP002921486<br>* the whole document *  | 46, 47   |  |
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| The present search report has been drawn up for all claims  |  |  | TECHNICAL FIELDS SEARCHED (Int.Cl.6)         |
| Place of search<br>MUNICH   |  | Date of completion of the search<br>10 November 2003 | Examiner<br>Madlener, M                      |
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|  |   |   | TECHNICAL FIELDS SEARCHED (Int.Cl.6)         |
| The present search report has been drawn up for all claims   |   |   |  |
| Place of search<br><b>MUNICH</b>   |   | Date of completion of the search<br><b>10 November 2003</b> | Examiner<br><b>Madlener, M</b>               |
| <p><b>CATEGORY OF CITED DOCUMENTS</b></p> <p>X : particularly relevant if taken alone<br/>Y : particularly relevant if combined with another document of the same category<br/>A : technological background<br/>O : non-written disclosure<br/>P : intermediate document</p> <p>T : theory or principle underlying the invention<br/>E : earlier patent document, but published on, or after the filing date<br/>D : document cited in the application<br/>L : document cited for other reasons<br/>&amp; : member of the same patent family, corresponding document</p> |   |   |  |

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Application Number  
EP 99 11 2181

**CLAIMS INCURRING FEES**

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

**LACK OF UNITY OF INVENTION**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:





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**LACK OF UNITY OF INVENTION  
SHEET B**

Application Number  
**EP 99 11 2181**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

**1. Claims: 1-32**

Processes for - linearly or non-linearly - amplifying a specific nucleic acid sequence involving a primer comprising two segments inducing, e.g., hairpin formation during the extension reaction, subsequent binding of a second primer, second primer extension, and displacement of the first primer extension.

**2. Claims: 33-45**

Post-termination labelling process involving the incorporation of terminators.

**3. Claims: 46-47**

Process for producing nucleic acid sequences having decreased thermodynamic stability to complementary sequences and single- or double-stranded nucleic acid polymers involving at least one modified nucleotide (analog) comprising a negatively charged chemical moiety.

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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